our case report and quoted two additional cases of the NMS which responded to amantidine.

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Crohn's colitis and sarcoidosis

Sir,

The similarities between Crohn's disease and sarcoidosis were emphasized in the case reported by Dr McCormick and his colleagues.[1] Cases of Crohn's disease sometimes show positive Kveim tests,[2] and the disorder is, at times, indistinguishable from ulcerative colitis.[3] BCG inoculation may also conceivably account for the apparent increase in its incidence.[4] The difference between Crohn's disease and sarcoidosis is slight, and it is probably due to slightly different transmissible agents. Sarcoidosis is possibly due to an attenuated human mycobacterium, while Crohn's disease may be caused by a bovine and attenuated mycobacterium.

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Fansidar – a treatment for AIDS-related pneumocystis?

Sir,

The standard treatment of acquired immune deficiency syndrome (AIDS) associated *Pneumocystis carinii* pneumonia (PCP) is high dose co-trimoxazole (trimethoprim and sulphamethoxazole).[1] This drug results in a severe hypersensitivity reaction in more than 50% of patients. Pentamidine is an established alternative, but poor patient tolerance is common and the intramuscular route is contraindicated in thrombocytopenia. Low dose Fansidar (one tablet weekly of pyrimethamine 25 mg, sulfadoxine 500 mg) has been used as an alternative agent to co-trimoxazole in prophylaxis against recurrence of AIDS-related PCP.[2] We describe here the apparently successful use of high dose Fansidar (three tablets weekly) in the treatment of PCP in three patients intolerant of co-trimoxazole.

Comparative details of the three patients are given in Table I. All patients were human immunodeficiency virus (HIV) antibody positive and PCP was confirmed using trans-bronchial biopsy or lavage. All patients were treated initially with co-trimoxazole. In each case, a hypersensitivity rash appeared between 5 and 12 days following introduction of the drug. Patient 1 also received trimethoprim, which again resulted in a hypersensitivity rash. None of the patients received post-PCP prophylaxis or folic acid supplements.

None of our patients treated with Fansidar has suffered a relapse of their PCP over a period of at least 3 months in spite of not receiving prophylaxis. This is surprising in a disease exhibiting a median survival time of 9 months but may partly reflect the long half-life of Fansidar (130 hours).

Fansidar is not without side effects. These include elevation of liver enzymes and occasionally hepatitis; the former we saw in patient 1, who had the longest period of treatment. Marrow suppression may also occur, resulting in agranulocytosis, perhaps related to changes in folic acid metabolism. Patients 1 and 3 had falls in cell counts. Close monitoring of chemistry and haematological parameters is recommended.

Cutaneous adverse reactions, including Stevens-Johnson syndrome, have also been reported.[3] However, in limited and cautious use, 75% of patients reacting to co-trimoxazole could tolerate Fansidar.[4] This observation and the reaction of our patient 1 to trimethoprim suggest that the constituent sulphonamides are not always the problem and that some AIDS patients may be specifically intolerant of trimethoprim.

It can be argued that the clinical improvements seen in our patients were a delayed response to prior therapy. However, the symptomatic improvement (and radiological clearing in patients 1 and 3) seen only after starting Fansidar may be significant. Certainly a controlled comparative trial of co-trimoxazole and Fansidar is warranted. Until then we consider that Fansidar is worth trying in the treatment of life-threatening PCP, particularly in patients sensitive to or intolerant of co-trimoxazole and pentamidine.

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Table I Patient details

	Patient 1	2	3
Age	31	43	46
Sexual preference	bisexual	bisexual	homosexual
Days of co-trimoxazole treatment	5	12	8
Reason for stopping	rash	nausea rash	rash pruritus
Doses of Fansidar	10	4	6
Reason for stopping	improved	nausea	improved
Hepatic enzymes	increase	no change	no change
Chest X-ray	improved	no change	improved
Months off treatment	9	6	3

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Clomiphene citrate in Tourette's syndrome

Sir,

We have recently successfully treated a 39 year old man with Tourette's syndrome using the anti-oestrogenic agent, clomiphene citrate (Clomid[R]). The patient exhibited motor and phonic tics associated with obsessive-compulsive behaviour, deviant sexual behaviour and sleep disturbances since the age of 7 years. Over the past few years he had experienced frequent unpleasant, sexually-oriented dreams.The patient's symptoms were unresponsive to administration of haloperidol (dose range: 2–20 mg/day), diazepam (10–40 mg/day), clonidine (0.1–0.3 mg/day), clonazepam (1–4 mg/day) and chlorpromazine (25–75 mg/day). A recent neurological evaluation disclosed severe motor tics that involved the neck and shoulder muscles and, to a lesser extent, the extremities. In addition, he was frequently grunting and sniffing. Vocalizations were only noted during extreme mental excitement.

Based on recent evidence implicating deranged gonadotrophic functions in Tourette's syndrome,[1] we measured plasma luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels pre- and post-luteinizing hormone releasing hormone (LHRH) stimulation (100 μg s.c.). While baseline plasma LH levels were low (2.2 IU/l/ml), FSH levels were in the normal range (6.7 IU/l/ml). Following LHRH stimulation (after an overnight fast), LH levels rose to a peak of 108.6 IU/l/ml within 60 minutes, while FSH levels rose only moderately to 12.7 IU/l/ml at the same time. Baseline plasma testosterone levels were in the normal range (7.1 ng/ml). These findings suggested hypothalamic-mediated LHRH deficiency. After receiving informed consent from the patient and approval to proceed by the Human Subjects Committee, the patient was placed on clomiphene citrate (25 mg twice daily). Following one week of therapy, there was a dramatic reduction in the severity and, to a lesser extent, in the frequency of the motor and phonic tics. This was supported by a blinded videotape evaluation by two independent neurologists. In addition, the patient appeared relaxed, less depressed and also reported experiencing more pleasant, sexually-oriented dreams and an improvement in his sleep onset and duration. Paradoxically, plasma LH levels were undetectable, while FSH levels rose to 16.8 IU/l/ml. Testosterone levels rose slightly to 8.9 ng/ml within one week of therapy.

Clomiphene citrate, a non-steroidal oestrogen, has been shown to inhibit competitively oestradiol binding to oestrogen receptors in the rat pituitary and hypothalamus, suggesting that it acts as an anti-oestrogen.[2] Other workers have suggested that clomiphene, like oestradiol, acts by increasing the responsiveness of gonadotrophs to LHRH.[3] More recently, Kerin *et al.*[4] provided evidence to suggest that clomiphene acts at a hypothalamic site by inducing an increase in the frequency of LHRH release. Whatever the mechanism of action of clomiphene in our patient may be, improvement of symptoms was accompanied by a depression of LH, elevation of FSH and testosterone levels, suggesting that his baseline abnormal gonadotrophin functions were somehow linked to the clinical expression of his disorder. Moreover, the supramaximal response of LH to administration of LHRH in our patient suggests the presence of supersensitive LHRH receptors in the hypothalamic-pituitary axis and further supports the clinical evidence for deranged hypothalamic functions in Tourette's syndrome.[5]

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